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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,169	06/08/2001	Clemens Antoni Van Blitterswijk	04148-00012	9604

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EXAMINER

DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,169	VAN BLITTERSWIJK ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10,13,14,16-18,20-23,25,26 and 28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.

- 6) ☒ Claim(s) 10,13,14,16-18,20-23,25,26 and 28 is/are rejected.

- 7) ☐ Claim(s) _____ is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/621178 08/810266.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

Status of Application, Amendments and/or Claims

The amendment filed 16 October 2003 has been entered in full. Claims 15, 19, 24 and 27 were cancelled. Claims 10, 13, 14, 16-18, 20-23, 25, 26, and 28 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 10, 13-19 under 35 USC 112, first paragraph, written description, new matter, as set forth at page 3 of the previous Office Action (29 July 2003) is *withdrawn* in view of Applicants' argument (16 October 2003).

The rejection of claims 10, 13-16, 18, 20, 22 and 23 under 35 U.S.C. 102(b) as being anticipated by Gazit *et al.*, Connective Tissue Research, Vol. 23, pages 153-161, 1989 as set forth at pages 4-5 of the previous Office Action (29 July 2003) is *withdrawn* in view of Applicants' arguments (16 October 2003).

The rejection of claims 25, 26 and 28 under 35 U.S.C. 102(b) as being anticipated by Gleave *et al.*, The Journal of Urology, Vol. 147, 1151-1159, 1992 as set forth at pages 5-6 of the previous Office Action (29 July 2003) is *withdrawn* in view of Applicants' arguments (16 October 2003).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 13, 14, 16-18, 20-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of producing osteocalcin comprising the steps of (a) applying bone marrow cells on a substrate

(b) contacting the bone marrow cells with a culture medium

(c) inducing the bone marrow cells to differentiate into osteogenic tissue by one or more inductors of differentiation, wherein osteogenic tissue produce osteocalcin

(d) recovering osteocalcin from the culture medium,

does not reasonably provide enablement for:

a method of producing active factors (or bone growth factor) comprising the steps of (a) applying undifferentiated mammalian cells on a substrate

(b) contacting the undifferentiated mammalian cells with a culture medium

(c) inducing the undifferentiated mammalian cells to differentiate by one or more inductors of differentiation. wherein differentiated cells produce active factors (or bone growth factors)

(d) recovering the active factors (or bone growth factors) from the culture medium. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The scope of patent protection sought by Applicant as defined by the claims fails to bear a reasonable correlation with the scope of enabling disclosure set forth in the

specification because the instant claims broadly encompass any type of undifferentiated mammalian cell and the recovery of any growth factor, bone formation factor, bone cell proliferation factor, bone cell adhesion factor, cell proliferation factor and cell adhesion factor from any type of undifferentiated mammalian cells.

The instant specification teaches that rat bone marrow cultured in medium develop into opaque, three dimensional mineralized nodular structures after two weeks (page 5, lines 1-16). The specification states that the osteogenic character of rat bone marrow culture system has been well characterized using a number of criteria (page 5, lines 21-34). Example 1 lists the criteria. The specification teaches that the osteocalcin bone protein is released in the medium (page 6, lines 4-5 and page 12, lines 15-16). The instant specification does not teach that any type of undifferentiated mammalian cell can be made to differentiate and produce active factors. The specification fails to disclose a criterion to discern a specific differentiated cell besides osteogenic characteristics of bone marrow cells. Furthermore, the types of factors recited in the claims are very diverse. One skilled in the art would need to employ different assays for recovery and to discern activity. The specification fails to disclose assays or experiments to discern activity or distinguish between types of factors. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Due to the large quantity of experimentation necessary to induce undifferentiated mammalian cells to differentiate wherein growth factors, bone formation factors, bone

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cell proliferation factors, bone cell adhesion factors, cell proliferation factors, and cell adhesion factors can be recovered from differentiated mammalian cells and possibly screen for activity of said factors, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding types of undifferentiated mammalian cells and active factors which can be recovered, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 25, 26, 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of producing growth factors comprising the steps of (a) applying stromal cells on a substrate, (b) contacting the stromal cells with a culture medium, (c) inducing the stromal cells to differentiate by one or more inductors of differentiation, wherein differentiated cells produce growth factors, (d) recovering the growth factors from the culture medium.

The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure because the instant specification only teaches the

use of bone marrow cells in the claimed method. Stromal cells and bone marrow cells are different types of tissues. The specification fails to teach the differentiation of stromal cells and the recovery of various factors from differentiated cells. The specification also fails to disclose the criteria for discerning differentiation of stromal cells. As was stated above, the instant claims encompass the recovery of every type of growth factor, bone formation factor, cell proliferation factor and cell adhesion factor from cultured stromal cells.

Due to the large quantity of experimentation necessary to induce stromal cells to differentiate wherein growth factors, bone formation factors, cell proliferation factors, and cell adhesion factors can be recovered from differentiated stromal cells and possibly screen for activity of said factors, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding factors which can be recovered, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



RMD
January 10, 2004



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